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Possible reasons would be (1) a longer follow-up period and more cases in the 1984 report than in the 1981 report, or (2) husbands' age and occupation were standardized for data in 1981, while data reported in 1984 was standardized by age only. However, the latter is definitely not the reason responsible for the discrepancy, as age-occupation standardized data in 1984 showed almost similar results, corresponding relative risks (r.rs) being 1.00, 1.11, and 1.36 (trend p : 0.009), respectively (Table 1). The results were also similar when standardized by wives' age, corresponding r.rs being 1.00, 1.09, and 1.34 (trend p : 0.019). Therefore, it should be concluded that the more cigarettes the husbands smoke, the higher the ischemic heart disease risk in nonsmoking wives.

In 1980-1981, r.rs of ischemic heart disease in nonsmoking wives were 1.00, 1.29, and 1.87 (trend p : 0.041) when husbands were nonsmokers, exsmokers/10-19 daily, and 20+ daily respectively. One may further consider as the possible reasons for this discrepancy the influence of the changing quality of side-stream smoke coming out of the ignited end of cigarettes in recent years due to the intensive chemical manipulation of the products (e.g., inclusion of tobacco additives) in order to lower tar and nicotine, to improve the flavor, etc. Also, the recent increase in fat consumption in Japan may interact on the risk of ischemic heart disease when exposed to passive smoking.

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REBUTTAL TO LEE/KATZENSTEIN COMMENTARY ON PASSIVE SMOKING RISK

Dear Editor:

Lee (1989) and Katzenstein (1989), in their commentary on Wells'(1988) paper, take issue not only with Wells' estimates of the magnitude of the mortality effect of passive smoking on nonsmokers, but question whether mortality occurs at all. Their arguments are based upon the alleged fragility of the epidemiological studies of passive smoking and disease; the potential for misclassification of subjects, disease, or exposure; possible confounding factors; and the lower doses of smoke to which nonsmokers are exposed relative to smokers.

Let us examine these issues one by one. Are nonsmokers exposed to such low doses of environmental tobacco smoke (ETS) that Wells' estimates of 46 000 nonsmokers' deaths per year from passive smoking are about "46 000 too high", as Lee asserts? Perhaps the most salient point to be considered: active smoking is a cause of more than one out of every six deaths in the U.S.A. every year (USSG 1989). Intentional exposure to tobacco smoke has been judged to cause coronary heart disease, atherosclerotic peripheral vascular disease, lung and laryngeal cancer, oral cancer, esophageal cancer, chronic obstructive pulmonary disease, chronic bronchitis, intrauterine growth retardation, and low birthweight babies. In addition, probable causality has also been established for unsuccessful pregnancies, increased infant mortality, and peptic ulcer disease, as well as cancers of the bladder, pancreas, and kidney, and associations have been reported for cancer of the stomach (USSG 1989). Hardly an organ system of the human body remains undiseased upon exposure to tobacco smoke. To argue, as do Lee and Katzenstein, that the diseases of smoking are not even plausible in nonsmokers does not give us confidence in their deductive abilities. To be sure, it is possible that thresholds for effect may exist for one or more of the diseases of smoking, but neither Lee nor Katzenstein present any evidence whatsoever that such low dose thresholds exist, let alone that all nonsmokers have exposures and susceptibilities which place them within an adequate margin of safety below such thresholds.

Are the epidemiological studies of passive smoking and lung cancer really all to be explained by misclassification of smokers as nonsmokers as Lee has proposed? Nonsmokers who report no passive smoking nevertheless possess levels of nicotine and cotinine in body fluids which are significant fractions of those who report a lot of exposure. For

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example, of 100 nonsmokers studied by Jarvis (1987), the 46% who reported "no" exposure had measured urinary cotinine levels which were nearly a third of the levels of those 27% of nonsmokers who reported "some" or "a lot" of passive smoking exposure. This suggests that there is major misclassification of nonsmoking controls as "unexposed". The result of this kind of misclassification of nonsmokers is to cause epidemiological studies to lack statistical significance or to find no effect. Nevertheless, despite such misclassification of controls, fully two-thirds of the studies shown by Katzenstein in his Table 1 showed a positive result.

Are confounding factors such as higher exposure to carcinogenic organic chemicals from non-ETS sources in the spouses of smokers, as Katzenstein asserts, really responsible for the consistent reports linking lung cancer to passive smoking from 15 different researchers in six different countries? To the contrary: Wallace (1989), in making measurements of personal exposure to benzene, a known human carcinogen and a prominent constituent of tobacco smoke, found that benzene exposures were 50% higher in the nonsmoking children and spouses of smokers than for nonsmokers in nonsmoking households.

Finally, what of the magnitude of Wells' (1988) estimates which Lee asserts are 46 000 too high? Let us take lung cancer, which Wells has estimated at 3000 U.S. lung cancer deaths (LCDs) per year. Lee selectively contrasts the estimate of 12 LCDs/yr from passive smoking by Arundel et al. (1987), but omits the mention of eight other risk assessments with which Wells' assessment agrees, all eight of which taken together average 5000 ± 2400 LCDs/yr. (Repace and Lowrey 1990). It is Arundel et al. who are out of step with the rest, not Wells. This lends credence to Wells' risk assessment methodology.

As far as heart disease mortality is concerned, this is primarily a disease of those aged ≥ 35 years. In 1985 there were roughly 105 million Americans in this age bracket, roughly 72 million nonsmokers, and 33 million smokers. Among the 33 million smokers, there were 120 000 active smoking-attributable heart disease deaths (HDDs) in 1985, or 3.6×10^{-3} HDD/smoker. By comparison, Wells' estimates 32 000 passive smoking-attributable nonsmokers' HDDs per year in a population of 72 million, or 4.4×10^{-4} HDD/nonsmoker. Thus, the ratio of ETS-induced heart disease deaths per nonsmoker to smoking-induced heart disease deaths per smoker is only 12%, which does not seem excessive considering that tobacco smoke is known to be one of three major risk factors for HDD, and synergistic (USSG 1989) with the other two factors (hypertension and elevated serum cholesterol) which are also common in nonsmokers.

A final note on Katzenstein's attack on the risks of passive smoking-induced lung cancer death (LCD) estimated by Repace and Lowrey (1985, 1986, 1987). The radical difference in lifestyle between never-smoking Seventh Day Adventist (SDA) controls and never-smoking non-SDAs is the avoidance of passive smoking in the SDA lifestyle, which we believe convincingly accounts for their lower lung cancer rate. As Katzenstein selectively notes, we were criticised by OTA (1985) and by tobacco industry consultants for attributing the entire LCD rate difference to passive smoking, but what our critics have conveniently ignored is that, since 60% of the SDA control group were potentially exposed to passive smoking, this was in fact a conservative estimate. Moreover, Katzenstein selectively omits mention of the analysis of our work by Weiss (1986), who found our figures to be "the best current estimates of lung cancer deaths from passive smoking".

In sum, contrary to the assertions of Lee and Katzenstein, we find Wells' predictions of 46 000 deaths per year from passive smoking to be credible, and to indicate, as Wells concluded, that exposure to ETS can have adverse long-term health effects that are more serious than previously thought.

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AN ESTIMATE OF ADULT MORTALITY IN THE UNITED STATES FROM PASSIVE SMOKING; A RESPONSE

Dear Editor:

An article in Inside EPA (January 13, 1989) is headlined: "EPA weighs Impact of Study Linking Passive Smoke Exposure to Heart Deaths . . ." It leads with the statement: "EPA is giving serious attention to a recently published study that pinpoints passive smoking . . . as a significant cause of heart disease and cancer-related deaths". The article states: "Passive smoking causes 46 000 deaths a year, according to a study by A. Judson Wells published last month in *Environment International*". An EPA source is quoted: "The 46 000 mortality was surprising because such a large component was from heart disease . . ." This statement is similar to one made by EPA's James Repace on national television when the report was first released.

What is surprising is that anyone from the EPA can consider this recent review surprising. Dr. Wells has not completed an epidemiological study, new or otherwise, and has in no way contributed to pinpointing passive smoking as a significant cause of heart disease, lung cancer, or other cancer deaths. What he did was publish the results of a series of calculations based on the results of existing epidemiological studies and a number of assumptions (Wells 1988). Dr. Wells presented a similar analysis at the 1986 Air Pollution Control Association meeting, which was published in the meeting proceedings (Wells 1986). There should have been no sudden surprise at EPA; an EPA official chaired the 1986 session in which this paper was presented. Dr. Wells encourages the view that he had done something new by failing to even acknowledge his previous presentation.

Wells used the data of previously published (and in some cases, unpublished) studies as a basis for calculating annual mortality statistically associated with ETS exposure. These calculations do not in any way establish that ETS does, in fact, cause death in exposed individuals. Rather, such calculations rely on an independent conclusion, based on a review of the available data, that ETS causes lung cancer, other cancers, and cardiovascular diseases. If such a conclusion cannot be supported, then the estimate of ETS-associated mortality rests on the assumption that ETS causes these diseases, and it is incumbent upon the author to state this underlying assumption when reporting the results of his calculations.

The issue of causation is never addressed by Wells. The studies cited in Wells' Tables 1-4 are discussed below with particular attention to whether they establish a causal relationship between ETS and disease in non- or never-smokers. The vast majority of the studies were included in reviews published by the National Academy of Sciences (NAS 1986) and the Surgeon General (USSG 1986). Therefore, these reports are used as a starting point for addressing the question of causality.

Lung Cancer: Almost all of the epidemiological studies listed in Wells' Tables 1 and 2 were considered in the NAS and Surgeon General's reports, as well as other reviews appearing at about the same time (Blot and Fraumeni 1986; Überla 1987). The Surgeon General's Report was alone in concluding that ETS causes lung cancer in nonsmokers; the other reviews generally concluded that although a statistical association appeared to exist between marriage to a smoker and the risk of lung cancer, the lack of adequate exposure information, and the potential influence of differential misclassification of smoking status precluded a conclusion of causality. The lung cancer studies published since these reviews have the same limitations as the previous studies. Little has been published since 1986 that adequately addresses the issues of exposure and misclassification.

All of the studies attempting to link cancer to ETS have been epidemiological. An epidemiology study attempts to relate the frequency of a certain health effect or disease with the frequency of specific envi-

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